Feline hypersensitivity dermatitis

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TREATMENT OF FELINE HYPERSENSITIVITY DERMATITIS

CYCLOSPORINE

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Treatment of hypersensitivity disorders in cats is mainly based on the use of glucocorticoids and cyclosporine. As the former drugs are already weel-known from most practionners, this text will focus on cyclosporine. The other drugs will be mentioned during the lecture.

Cyclosporine A (CsA) is an immunomodulatory drug belonging to the group of calcineurin inhibitors. This lipophilic drug penetrates easily the cell membranes and binds in the cytoplasm to cyclophiline. CsA-Cyclophiline complex inihibits calcineurin, leading to an impaired activation of Nuclear Factor of Activated T cells (NF-AT). As NF-AT is one of the major activator of cytokine genes transcription, CsA administration results in an impaired expression of cytokines.

At the cellular level, CsA inhibits T lymphocyte activation, eosinophil recruitement, functions and growth of antigen-presenting cells, especially Langerhans cells, pro inflammatory cytokines secretion of keratinocytes and IgE mediated mast cell degranulation.

After oral or intravenous administration, peak and trough levels are highly variable in cats. It has however been shown that serum concentration and clinical efficacy are not correlated which implies that routine evaluation of CsA blood concentration is not necessary, in most occasions. The peak concentration is obtained one hour after oral administration of 5mg/kg CsA and ranges between 100 and 1600 ng/ml when measured by high-pressure liquid chromatography. It is worth noticing that CsA values depend on the technique used and immunoassays provided usually much higher values, when compared with high pressure chromatography.

The bioavailability of CsA in cats is rather low (29%) and bioaccumulation is usually not observed. As mentioned above, CsA is a very lipophilic drug, which explains the high volume of distribution (6L/kg) as well as the high concentration in the skin (4 times higher than in serum). Feeding before CsA administration is associated with a lower bioavailability but this decrease does not seem to impair clinical outcomes.

CsA interacts with cytochrome P 450 3A4 and drug interactions are consequently numerous. Very few have however been demonstrated in clinical study and these interactions may be influenced by several factors such as age, concurrent diseases, dosage etcŭ In cats, interaction between CsA and ketoconazole, itraconazole and clarythromycine have been demonstrated. Concomitant treatment should be

associated with a reduction of CsA administration. Other possible interaction with ranitidine, omperazole, cimetidine, metoclopramine, allopurinol, erythromycin, digoxine, furosemide, ciprofloxacine, verapamil and trimethoprim- sulfa are likely.

Side-effects of CsA include gastrointestinal signs, anorexia, weight loss and gingivitis. Otitis and cystitis are also sometimes observed during CsA treatmenteven though causality is not firmly established [1,2]. Outdoor cats should also be tested for toxoplasma IgG before treatment and negative cats should not be treated or should be kept indoors during the whole treatment. On the contrary, IgG positive cats are protected. As well, cats with chronic infectious diseases such as FIV, FeLV, dermatophytosis should not be treated with CsA. Cats with chronic kidney deficiency and diabetes mellitus could treated with CsA but should be monitored carefully.

In a Novartis intern study (freedom of information), cats were first vaccinated and, then, treated 4 months afterwards with CsA 24mg/kg during 8 weeks. These cats were subsequently re-vaccinated after this period of treatment: Titers were lower than in the control group but still in normal range which suggests that booster vaccination could be made during CsA treatment.

The first evidence for the efficacy of CsA for the treatment of hypersensitivity cats was provided by an open study published by Noli and coworkers [3]. The first controlled study was published by Wisselink and coworkers who compared two groups of allergic cats, the first one being treated with CSA 5 mg/kg and the second one with Prednisolone 0.5mg/kg. Improvement of the clinical signs were seen in both groups [4]. Larger studies were published afterwards and evidence was provided that the better dosage for allergic cats was 7 mg/kg [2]. Some other studies were carried out afterwards but are still not published. It was however demonstrated that after an initial phase of treatment of 6 to 8 weeks, about 70% of allergic cats only need every other day treatment. After 4 additional weeks, 55 % were treated only twice a week while 20 % were still on every other day treatement and 15% on daily administration. Only 10% did not respond to the treatment.

All in all, studies show that CsA is a good treatment option for allergic cats and that most of them support the treatment well.

References

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